

## **REMARKS**

### **Status of the Claims**

Claims 1-3 and 9 are pending. Claims 1-3 have been amended. Claim 7 has been canceled. Claims 4-6 and 8 were canceled previously. New claim 9 has been added.

### **Amendments to the claims**

Claim 1 has been amended to delete the second alternative where SEQ. ID NO: 70 and SEQ. ID NO: 71 are alternately chemically bonded. This subject matter is now recited in new independent claim 9. Also a limitation pertaining to the support being 'essentially of nylon' has been deleted. Dependent claims 2 and 3 have been amended to add additional dependencies. No new matter was added.

### **Rejections under 35 U.S.C. §103(a)**

Claims 1-3 and 7 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Hillegas (US Patent 6,214,618 B1) in view of Ferrari (US Patent 6,184,348 B1), Aerts (WO2004/078955 A1) and Cherksey (US Patent 5,618,531). Applicants respectfully traverse this rejection.

According to the Examiner, Hillegas teaches methods of producing herpes virus comprising adhering cells to a micro carrier support comprising multiple copies of the cell attachment ligand, Arg Gly Asp (RGD) (the fibronectin cell binding domain) peptide citing claims 1-13, column 2, lines 19-41, column 3, lines 15-27, column 4, lines 35-62, and Example 2. However, claims 1-13, column 2, lines 19-41, do not mention fibronectin or Arg Gly Asp (RGD) peptide. In the background section of Hillegas, column 3, lines 15-27 the brand name protein Pronectin F having multiple copies of the cell attachment ligand (RGD) is mentioned. Column 4, lines 35-62, and Example 2 of Hillegas mention Pronectin-F as one of the several natural or synthetic proteins that may be used for coating the microcarrier beads of the invention.

The Examiner presents the above description in the specification of Hillegas divorced from the primary teachings of Hillegas, which pertain to producing microcarrier beads made of a lightly cross linked styrene copolymer core and also having functional groups, especially trimethylamine group (TMA), on the surface of the bead and washing the microcarrier beads with basic and acidic solutions to make the beads compatible for cell culture (see abstract and

summary, Hillegas). Hillegas teaches that such lightly cross linked styrene copolymer core allows the bead to remain autoclavable and provides a better cell binding surface and the TMA group on the surface of the bead facilitates cell attraction and attachment because its cationic amine functionality.

Claims 1-13 of Hillegas pertain to the specific styrene copolymer microbeads with TMA exterior and their washing with basic and acidic solutions. Hillegas presents coating these micro beads with a natural or synthetic protein as a further option without any emphasis on either the coating or the type of coating:

Additionally, the TMA microcarrier bead can be further coated, if important to a specific cell culture. This coating can include, but is not limited to, porcine, bovine or human collagen, or ProNectin-F, (a recombinant fibronectin-like moiety) or other natural or synthetic peptides. (Hillegas; Column 4, lines 48-52) (emphasis added)

It is notable that Hillegas provides no preference for ProNectin-F over porcine, bovine or human collagen protein coating which have animal origins. Similar optional use of ProNectin-F is disclosed at column 3 line 66 to column 4, line 2; and Column 6, lines 25-31 of Hillegas.

Given this disclosure in Hillegas, the person of ordinary skill in the art would not be motivated to start with Hillegas and modify it with the teachings of Ferrari or Cherksey. Hillegas promotes the use of TMA or similar functional groups at the surface of lightly cross linked styrene copolymer to improve cell attachment and provides no incentive to modify the coating protein, which is presented as an optional variant.

Even if, assuming for the sake of argument, the person of ordinary skill in the art were to start with Hillegas and combine it with teachings of Ferrari, Aerts and Cherksey, the result would not be the method of the instant invention. The Examiner asserts that Ferrari teaches polymer polypeptides Gly Ala Gly Ala Gly Ser (GAGAGS) and Arg Gly Asp (RGD) peptide bonded together in a tandem repeat citing claims 4 and 5 of Ferrari, and that Ferrari teaches that the polymer peptide contains repeating units of Gly Ala Gly Ala Gly Ser (GAGAGS) and Arg Gly Asp (RGD) citing claims 1-14.

Applicants respectfully submit that the Examiner's reading of Ferrari is flawed. Claim 1 of Ferrari pertains to a proteinaceous polymer "that comprises strands of repeating units of a natural protein capable of assembling into aligned structures to be formable into articles, wherein at least one of said strands comprises a tandem repeat of said repeating units, with at least two

strands joined by an intervening oligopeptide other than said repeating units. Dependent claim 4 recites RGD as an intervening oligopeptide and dependent claim 6 calls for GAGAGS as a strand of repeating units. Dependent claim 5 allows for an option where the polymer is a block copolymer with two different repeating units. Claims 11 and 14 call for the intervening sequence to have binding specificity for a protein receptor. Arg Gly Asp, or RGD has binding specificity for a protein receptor. It is clear from a plain reading of the description and claims of Ferrari that Arg Gly Asp is taught as an intervening oligopeptide or sequence in Ferrari while the strand comprising tandem repeats of repeating units may be of GAGAGS repeating units, either alone or as block copolymers with other repeating units such VPGVG, GPP or GAP (see claim 6). Also, the specification and claims of Ferrari clearly state that the intervening oligopeptide is other than or different from the repeating units (see, claims 1, 6, and column 3 lines 17-23). Ferrari does not suggest anywhere that the repeating units and the intervening oligopeptide can be the same or can be interchanged such that the sequences that are used as intervening oligopeptides for joining the repeating units can instead become a repeating unit themselves.

Thus, Ferrari does not teach a polymer polypeptide with GAGAGS and RGD bonded together in a tandem repeat, or a polymer peptide containing repeating units of GAGAGS and RGD. The sequence listings of Ferrari further confirm this reading where no alternate repeating units of GAGAGS and RGD can be found. The present application involves a polymer peptide which has five GAGAGS sequences and five RGD sequences alternately chemically bonded, a feature that is neither disclosed nor suggested by Ferrari.

Neither Aerts nor Cherksey cure this deficiency in Ferrari. Aerts and Cherksey do not teach or suggest polymer polypeptides with GAGAGS and RGD bonded together in a tandem repeat, or polymer peptide containing repeating units of GAGAGS and RGD. Aerts and Cherskey do not motivate a person of ordinary skill in the art to modify Ferrari or Hillegas to produce a polymer peptide containing five units of GAGAGS and five units of RGD, alternately chemically bonded. Therefore, the combination of Hillegas, Ferrari, Aerts and Cherksey do not render claim 1 obvious.

According to the Examiner, Aerts (WO 2004/078955 AI) qualifies as a prior art under 35 USC 102(a). The priority document shows that the present invention was invented at least on April 19, 2004, which is earlier than publication of Aerts on September 16, 2004. Applicants are herewith providing a certified translation of the priority document as **Exhibit A**, thereby

perfecting the priority. Accordingly, Applicants believe Aerts no longer qualifies as prior art under 35 USC 102(a).

In accordance with the above, Applicants assert that Hillegas, Ferrari, Aerts and Cherksey do not teach or suggest the subject of claim 1. Claims 2 and 3 are allowable for at least the same reasons as claims 1 and 9. The Examiner has cited no prior against the claimed method directed to a polypeptide where SEQ. ID NO: 70 and SEQ. ID NO: 71 are alternately chemically bonded. Therefore, Applicants believe new claim 9 is allowable. Claim 7 is canceled rendering that rejection moot. Applicants respectfully request that all rejections be withdrawn.

**CONCLUSION**

This amendment is believed to place the application in condition for allowance. If any issues remain which may be addressed by an Examiner's or supplementary amendment, the Examiner is respectfully requested to contact the undersigned.

Respectfully submitted,  
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Attachment as stated: **Exhibit A**

# EXHIBIT A